Cu-Catalyzed Asymmetric Allylic Alkylations of Aromatic and Aliphatic Phosphates with Alkylzinc Reagents. An Effective Method for Enantioselective Synthesis of Tertiary and Quaternary Carbons

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Supporting Information

General. Infrared (IR) Spectra are recorded on a Nicolet 210 spectrophotometer, ν_{max} in cm^{-1} . Bands are characterized as broad (br), strong (s), medium (m), or weak (w). ^1H NMR spectra are recorded on a Varian Unity INOVA 400 (400 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance resulting from incomplete deuteration as the internal standard (CDCl_3 : δ 7.26). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad and m = multiplet), coupling constants, and assignment. For products **5a** - **5i**, where a mixture of $\text{S}_{\text{N}}2'$ and $\text{S}_{\text{N}}2$ exists, data is presented only for the $\text{S}_{\text{N}}2'$ product in the ^1H NMR. ^{13}C NMR spectra are recorded on a Varian Unity INOVA 400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (CDCl_3 : δ 77.16). For products **5d**, **5h**, and **5i**, data is presented for the $\text{S}_{\text{N}}2'$ and $\text{S}_{\text{N}}2$ product mixture in the ^{13}C NMR. Enantiomer ratios are determined by chiral GLC analysis; (Alltech Associates Chiraldex GTA column (30 m x 0.25 mm)), Alphadex 120 column (30 m x 0.25 mm), or Betadex 120 column (30 m x 0.25 mm) or by analytical liquid chromatography (HPLC) on a Shimadzu chromatograph with a Chiralpak AS (4.6 x 250 mm) or a Chiralcel OJ (4.6 x 250 mm) chiral column by Chiral Technologies in comparison with authentic racemic materials. $\text{S}_{\text{N}}2':\text{S}_{\text{N}}2$ ratios are determined by achiral GLC analysis (J&W Scientific HP-5, 30 m x 0.25 mm) or by 400 MHz ^1H NMR. Elemental analyses are performed by Robertson Microlit Laboratories (Madison, New Jersey). High resolution mass spectrometry is performed by the University of Illinois Mass Spectrometry Laboratories (Urbana, Illinois) and by Mr. Chris Kowalczyk (on a Micromass LCT ESI-MS (positive mode)) at the Mass Spectrometry Facility, Boston College. Optical Rotation values are recorded on a Rudolph Research Analytical Autopol IV Polarimeter.

Unless otherwise stated, all reactions are conducted in oven (135 °C) and flame-dried glassware under an inert atmosphere of nitrogen. THF, Et_2O , and CH_2Cl_2 are purified through two alumina columns under a positive pressure of dry argon by a modified Advanced ChemTech purification system. Diethylzinc and dimethylzinc are purchased from Strem and used without purification. Other alkylzinc reagents are prepared according to known methods.¹ Copper (I) triflate (benzene complex, 2:1) is

¹ P. Knochel, R. Singer, *Chem. Rev.* **1993**, 93, 2177-2188 and references cited therein

prepared using known methods,² while copper (I) triflate (toluene complex, 2:1) is purchased from Aldrich and used without purification. Copper (I) cyanide is purchased from Strem chemicals and used without further purification. The allylic alcohols were prepared from the corresponding aldehydes and ketones by a two step Horner-Emmons olefination / LiAlH₄ reduction sequence,³ with the exception of compounds containing nitro groups and disubstituted *p*-CF₃ group, which were reduced using DIBAL-H. Allylic alcohols were converted to allylic phosphates using known procedures.³ EDC·HCl, HOBT·H₂O, DIC, piperidine, butylamine, DMF, Boc- and Fmoc-protected amino acids, and all salicyl aldehydes are purchased from commercial sources and used without further purification. Triethylamine is distilled from CaH₂. Gly-Wang resin (0.6 mmol/g) is purchased from Advanced ChemTech.

2-Hydroxy-1-naphthaldehyde- L-Asp (Ot-Bu)-L-Leu-NHn-Bu:

2-Hydroxy-1-naphthaldehyde- L-Asp (Ot-Bu)-L-Leu-NHn-Bu: Boc-L-Leu-OH (1.00 g, 4.0 mmol) is dissolved in 10 mL CH₂Cl₂ and HOBT·H₂O (0.61 g, 4.0 mmol) and EDC·HCl (0.76 g, 4.0 mmol) are added successively. The solution is cooled to 0 °C with an ice bath and *n*-butylamine (0.79 mL, 8.0 mmol) is added. The mixture is allowed to warm to room temperature and stir for 3 h. Reaction is quenched by addition of 20 mL 10 wt. % aqueous citric acid, and the solution is diluted by addition of 20 mL CH₂Cl₂. The organic layer is washed with 20 mL of a saturated aqueous solution of NaHCO₃ and 20 mL of a saturated aqueous solution of NaCl, dried over anhydrous MgSO₄, filtered and concentrated to yield a white solid.

Trifluoroacetic acid (2 mL) is added dropwise to Boc-L-Leu-NHn-Bu at 0 °C and allowed to stir for 30 minutes at which time the reaction is quenched by the dropwise addition of 2N aqueous solution of NaOH until the pH is >10. The aqueous solution is then washed with CH₂Cl₂ (3 x 10 mL). The organic layer is washed with 10 mL of a saturated aqueous solution of NaCl, dried over anhydrous MgSO₄, filtered and concentrated to afford H₂N-L-Leu-NHn-Bu (0.52 g, 2.8 mmol, 70%) as a yellow oil.

To a solution of H₂N-L-Leu-NHn-Bu (0.52 g, 2.8 mmol) and Fmoc-L-Asp (Ot-Bu)-OH (1.2 g, 2.8 mmol) in 7 mL CH₂Cl₂, HOBT·H₂O (0.43 g, 2.8 mmol) and EDC·HCl (0.53 g, 2.8 mmol) are added and the reaction is cooled to 0 °C with an ice bath. Et₃N (0.40 mL, 2.8 mmol) is added and the solution is allowed to warm to room temperature. The solution is allowed to stir for 12 h at which time the reaction is quenched by addition of 20 mL 10 wt. % aqueous citric acid and the resulting solution is diluted by addition of 20 mL CH₂Cl₂. The organic layer is washed with 20 mL of a saturated aqueous solution of NaHCO₃ and 20 mL of a saturated aqueous solution of NaCl, dried over anhydrous MgSO₄, filtered and concentrated to yield a white solid. Fmoc-L-Asp (Ot-Bu)-L-LeuNHn-Bu is dissolved in 10 mL CH₂Cl₂ and the flask is cooled to 0 °C. Piperidine (1.39 mL, 14 mmol) is added and the solids slowly dissolve. The mixture is allowed to stir at 0 °C for 30 minutes at which time the resulting solution is concentrated. The mixture is purified

² (a) R. G. Salomon, J. K. Kochi, *J. Am. Chem. Soc.* **1973**, *95*, 1889-1897. (b) R. G. Salomon, J. K. Kochi, *J. Am. Chem. Soc.* **1973**, *95*, 3300-3310.

³ C. A. Luchaco-Cullis, H. Mizutani, K. E. Murphy, A. H. Hoveyda, *Angew. Chem. Int. Ed.* **2001**, *40*, 1456-1460.

by silica gel chromatography (EtOAc to 10:1 EtOAc:MeOH) to yield the desired amine (0.73 g, 2.1 mmol, 75%).

H₂N-L-Asp (OtBu)-L-LeuNH*n*-Bu (0.79 g, 2.2 mmol) is dissolved in 5.5 mL CH₂Cl₂ and 2-hydroxy-1-naphthaldehyde (0.38 g, 2.2 mmol) is added followed by addition of anhydrous MgSO₄ (0.64 g, 4.4 mmol). The mixture is allowed to stir at room temperature for 12 h. At which time anhydrous MgSO₄ is filtered and the solution is concentrated to yield a light brown solid. The solid is purified by silica gel chromatography (1:1 hexanes:EtOAc, R_f product = 0.45) to yield a bright yellow solid (0.78 g, 1.5 mmol, 68%). mp 143-145 °C. IR (solid film): 3270 (br), 3081 (m), 2955 (m), 2917 (m), 2861 (w), 1728 (s), 1646 (s), 1539 (m), 1375 (m), 1155 (m), 834 (w), 746 (m) cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 9.27 (1H, s, HC=N), 8.06 (1H, d, *J* = 8.4 Hz, ArH), 7.83 (1H, d, *J* = 8.8 Hz, ArH), 7.75 (1H, dd, *J* = 8.0, 0.8 Hz, ArH), 7.53 (1H, ddd, *J* = 7.2, 7.2, 1.2 Hz, ArH), 7.36 (1H, ddd, *J* = 7.6, 7.6, 1.2 Hz, ArH), 7.14 (1H, d, *J* = 8.8 Hz, ArH), 6.53 (1H, d, *J* = 7.6 Hz, NH), 6.16 (1H, br s, NH), 4.45-4.37 (2H, m, NCHCO), 3.26-3.15 (2H, m, NCH₂), 3.13 (1H, dd, *J* = 16.4, 4.4 Hz, CHCHHCO), 2.81 (1H, dd, *J* = 16.4, 8.8 Hz, CHCHHCO), 1.77-1.54 (3H, m, aliphatic CH), 1.49-1.40 (2H, m, aliphatic CH), 1.36 (9H, s, *t*-Bu), 1.35-1.26 (2H, m, aliphatic CH), 0.94 (3H, d, *J* = 6.4 Hz, CH(CH₃)₂), 0.93 (3H, d, *J* = 6.4 Hz, CH(CH₃)₂), 0.88 (3H, dd, *J* = 7.2, 7.2 Hz, CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 171.5, 170.7, 170.1, 165.3, 165.0, 136.1, 133.1, 129.6, 128.4, 128.0, 124.0, 120.6, 119.0, 108.9, 82.0, 68.7, 52.5, 41.0, 40.1, 39.7, 31.8, 28.4, 25.3, 23.2, 22.5, 20.4, 14.0. HRMS Calcd for C₂₉H₄₁N₃O₅Na (M+Na⁺): 534.2942; Found: 534.2944. [α]_D²⁰ +3.5° (*c* = 0.87, CHCl₃).

Representative procedure for Cu-catalyzed allylic substitution of dialkylzinc reagents with unsymmetrical allylic phosphates. (CAUTION: Et₂Zn is pyrophoric! Use extreme caution!) In the glove box, a flask is charged with (40.2 mg, 8.00 × 10⁻¹ mmol) (CuOTf)₂ · PhH and (81.8 mg, 1.60 mmol) 2-hydroxy-1-naphthaldehyde-L-Asp(OtBu)-L-LeuNH*n*-Bu (**3**), sealed with a septum, and removed from the glovebox. Upon addition of 10.0 mL THF into the flask, the mixture is cooled to -15 °C in a dry ice/acetone bath and allowed to stir for 5 min before the addition of (500 μL, 4.80 mmol) Et₂Zn. A solution of 1-(2-nitrophenyl)-3-(diethylphosphoryloxy)-1-propene (504 mg, 1.60 mmol) in 10.0 mL THF is then added. The mixture is allowed to stir for 24 hours at -15 °C, at which time the reaction is quenched with the addition of 10 mL of a saturated aqueous NH₄Cl solution. The resulting solution is washed three times with 10 mL Et₂O and the combined organic layers are dried over anhydrous MgSO₄. The volatiles are removed *in vacuo* (CAUTION: Product is volatile!) to yield a yellow oil. The oil is purified by silica gel chromatography (100% pentane to 50:1 pentane:Et₂O to elute product) to yield the desired product as a light yellow oil (290 mg, 1.52 mmol, 95%).

(R)-(-)-3-Phenyl-1-pentene (9:1 mixture of S_N2' to S_N2 products). IR (neat): 3087 (w), 3069 (m), 2961 (s), 2924 (s), 2880 (m), 1645 (m), 1608 (m), 1495 (s), 1464 (s), 1382 (w), 916 (s), 696 (s) cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.36-7.18 (5H, m, ArH), 5.90 (1H, ddd, *J* = 17.2, 9.6, 7.2 Hz, CHCH=CH₂), 5.06-5.00 (2H, m, CHCH=CH₂), 3.14 (1 H, ddd, *J* = 7.2, 7.2, 7.2 Hz, CHCH=CH₂), 1.82-1.67 (2H, m, CHCH₂CH₃), 0.88 (3H, dd, *J* = 7.2, 7.2 Hz, CHCH₂CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 144.6, 142.4, 128.5, 127.8, 126.2, 114.2,

51.9, 28.5, 12.3. Anal Calcd for $C_{11}H_{14}$: C, 90.35; H, 9.65. Found: C, 89.99; H, 9.39. $[\alpha]_D^{20} -50.6^\circ$ ($c = 0.486$, $CHCl_3$) for a 95% ee sample. **Proof of Stereochemistry:** Literature value $[\alpha]_D^{20} +35.0^\circ$ ($c = 0.6$, C_6H_6) is assigned to the (*S*) enantiomer.⁴

The optical purity is determined by chiral GLC analysis (ChiralDEX-GTA, 45 °C, 15 psi); chromatograms are illustrated below:

Authentic racemic

Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	59.066	MF	1.4810	4.01000e5	4512.62500	48.54806
2	62.456	FM	1.9182	4.24986e5	3692.52686	51.45194

from catalytic reaction

Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	59.941	MF	1.2732	1.60202e5	2097.15918	97.69645
2	64.229	FM	1.0106	3777.34619	62.29582	2.30355

(*R*)-(-)-7-Methyl-3-phenyl-1-octene (6.7:1 mixture of S_N2' to S_N2 products). IR (neat): 3074 (w), 3059 (w), 3024 (m), 2955 (s), 2930 (s), 2880 (s), 1640 (w), 1596 (w), 1495 (m), 1470 (w), 1357 (w), 1004 (w), 910 (m) cm^{-1} . 1H NMR (400 MHz, $CDCl_3$): δ 7.37-7.18 (5H, m, ArH), 5.96 (1H, ddd, $J = 16.4, 10.8, 7.6$ Hz, $CHCH=CH_2$), 5.06-5.01 (2H, m, $CHCH=CH_2$), 3.25 (1H, ddd, $J = 7.6, 7.6, 7.6$ Hz, $CHCH=CH_2$), 1.74-1.15 (7H, m, aliphatic CH), 0.86 (3H, d, $J = 6.4$ Hz, $CH(CH_3)_2$), 0.85 (3H, d, $J = 6.4$ Hz, $CH(CH_3)_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.9, 142.7, 128.5, 127.7, 126.2, 114.0, 50.1, 39.0, 35.8, 28.0, 25.4, 22.8, 22.7. HRMS Calc for $C_{15}H_{22}$: 202.1721. Found: 202.1717. $[\alpha]_D^{20} -28.7^\circ$ ($c = 0.800$, $CHCl_3$) for a 91% ee sample.

The optical purity is determined by chiral GLC analysis (ChiralDEX-GTA, 60 °C, 15 psi, $t_{minor} = 269$ min, $t_{major} = 271$ min).

(*R*)-(-)-3-(4-trifluoromethylphenyl)-1-pentene (9:1 mixture of S_N2' to S_N2 products). IR (neat): 2962 (m), 2923 (m), 2873 (m), 1621 (m), 1332 (s), 1168 (s), 1130 (s), 1073 (s), 916 (m), 841 (m) cm^{-1} . 1H NMR (400 MHz, $CDCl_3$): δ 7.53 (2H, d, $J = 8.4$ Hz, ArH), 7.30 (2H, d, $J = 8.4$ Hz, ArH), 5.90 (1H, ddd, $J = 17.2, 10.4, 7.6$ Hz, $CHCH=CH_2$), 5.09-5.02 (2H, m, $CHCH=CH_2$), 3.21 (1H, ddd, $J = 7.6, 7.6, 7.6$ Hz, $CHCH=CH_2$), 1.84-1.67 (2H, m, $CHCH_2CH_3$), 0.87 (3H, dd, $J = 7.2, 7.2$ Hz, $CHCH_2CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.7, 141.4, 128.5, 128.2, 125.5 (q, $J = 3.4$ Hz, CF_3), 115.1, 51.7, 28.4, 12.2. HRMS

⁴ T. Hayashi, T. Hagihara, Y. Katsuro, M. Kumada, *Bull. Chem. Soc. Jpn.*, **1983**, 56, 363-364.

Calc for $C_{12}H_{13}F_3$: 214.0969. Found: 214.0969. $[\alpha]_D^{20} -35.4^\circ$ ($c = 1.03$, $CHCl_3$) for a 94% ee sample.

The optical purity is determined by chiral GLC analysis (α -dex, 80 °C, 15 psi); chromatograms are illustrated below:

Authentic racemic

Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	21.614	MM	0.1959	2.52163e5	2.14512e4	49.90828
2	22.279	MM	0.1997	2.53090e5	2.11210e4	50.09172

from catalytic reaction

Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	22.317	MM	0.1956	2.32963e5	1.98500e4	97.01960
2	23.038	MM	0.1885	7156.53760	632.60419	2.98040

(R)-(-)-7-Acetoxy-3-(4-trifluoromethylphenyl)-1-heptene (4.6:1 mixture of S_N2' to S_N2 products). IR (neat): 3075 (w), 2943 (s), 2861 (s), 1741 (s), 1621 (m), 1331 (s), 1256 (s), 1168 (s), 1123 (s), 1086 (s), 841 (m) cm^{-1} . 1H NMR (400 MHz, $CDCl_3$): δ 7.56 (2H, d, $J = 8.0$ Hz, ArH), 7.29 (2H, d, $J = 8.0$ Hz, ArH), 5.92 (1H, ddd, $J = 17.6, 10.0, 7.2$ Hz, $CHCH=CH_2$), 5.11-5.02 (2H, m, $CHCH=CH_2$), 4.03 (2H, dd, $J = 6.8, 6.8$ Hz, CH_2OAc), 3.31 (1H, ddd, $J = 7.6, 7.6, 7.6$ Hz, $CHCH=CH_2$), 2.02 (3H, s, CH_2OCOCH_3), 1.82-1.21 (6H, m, aliphatic CH). ^{13}C NMR (100 MHz, $CDCl_3$) (4.6:1 mixture of S_N2' : S_N2): δ 171.3, 171.3, 148.5, 141.2, 133.7, 129.1, 128.8 (q, $J = 32.2$ Hz, ArCCF₃), 128.5, 126.2, 125.8, 125.6 (q, $J = 3.8$ Hz, CF₃), 123.1, 120.4, 115.2, 64.6, 64.4, 49.7, 34.9, 33.0, 28.9, 28.6, 28.6, 25.6, 23.9, 21.1, 21.1. Anal Calcd for $C_{16}H_{19}F_3O_2$: C, 63.99; H, 6.38. Found: C, 63.64; H, 6.14. $[\alpha]_D^{20} -15.2^\circ$ ($c = 1.33$, $CHCl_3$) for a 84% ee sample.

The optical purity is determined by chiral GLC analysis (α -dex, 110 °C, 15 psi); chromatograms are illustrated below:

Authentic racemic

from catalytic reaction

Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	222.810	MF	2.2240	1.83413e5	1374.52429	50.85502
2	227.197	FM	2.7772	1.77245e5	1063.69702	49.14498

Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	226.019	MF	2.7031	2.28359e5	1407.99377	92.18112
2	232.520	FM	2.3500	1.93696e4	137.37326	7.81888

(R)-(+)-3-(2-Nitrophenyl)-1-pentene (4.9:1 mixture of S_N2' to S_N2 products). IR (neat): 3075 (w), 2967 (s), 2930 (m), 2873 (m), 1596 (m), 1608 (w), 1521 (s), 1357 (s), 922 (m), 853 (m) cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.72 (1H, dd, *J* = 8.4, 1.2 Hz, ArH), 7.55-7.50 (1H, m, ArH), 7.40 (1H, dd, *J* = 8.0, 1.6 Hz, ArH), 7.35-7.30 (1H, m, ArH), 5.92 (1H, ddd, *J* = 17.6, 10.4, 7.2 Hz, CHCH=CH₂), 5.12-5.05 (2H, m, CHCH=CH₂), 3.77 (1H, ddd, *J* = 7.2, 7.2, 7.2 Hz, CHCH=CH₂), 1.85-1.70 (2H, m, CHCH₂CH₃), 0.88 (3H, dd, *J* = 7.2, 7.2 Hz, CHCH₂CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 140.1, 132.5, 129.1, 127.0, 124.1, 116.0, 45.0, 28.4, 12.1. Anal Calcd for C₁₁H₁₃NO₂: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.07; H, 6.70; N, 7.32. [α]_D²⁰ +4.8° (*c* = 1.3, CHCl₃) for a 95% ee sample.

The optical purity is determined by chiral GLC analysis (Chiraldex-GTA, 130 °C, 15 psi); chromatograms are illustrated below:

Authentic racemic

from catalytic reaction

Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	15.762	MM	0.1523	1.29033e5	1.41222e4	50.77338
2	18.916	MM	0.2099	1.25102e5	9932.69141	49.22662

Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	15.436	MM	0.2474	9.08381e4	6119.30615	97.50281
2	18.213	MM	0.2471	2326.49634	156.92531	2.49719

(R)-(-)-7-Methyl-3-(2-nitrophenyl)-1-octene (6.7:1 mixture of S_N2' to S_N2 products). IR (neat): 3081 (w), 2955 (s), 2943 (s), 2867 (s), 1608 (m), 1527 (s), 1470 (m), 1350 (s), 922 (m), 784 (m),

746 (m) cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 7.71 (1H, dd, $J = 8.0, 1.2$ Hz, ArH), 7.55-7.50 (1H, m, ArH), 7.41 (1H, dd, $J = 8.0, 1.2$ Hz, ArH), 7.34-7.30 (1H, m, ArH), 5.93 (1H, ddd, $J = 17.6, 10.4, 7.6$ Hz, $\text{CHCH}=\text{CH}_2$), 5.12-5.04 (2H, m, $\text{CHCH}=\text{CH}_2$), 3.86 (1H, ddd, $J = 7.6, 7.6, 7.6$ Hz, $\text{CHCH}=\text{CH}_2$), 1.74-1.12 (7H, m, aliphatic CH), 0.83 (3H, dd, $J = 6.4$ Hz, $\text{CH}(\text{CH}_3)_2$), 0.83 (3H, dd, $J = 6.4$ Hz, $\text{CH}(\text{CH}_3)_2$). ^{13}C NMR (100 MHz, CDCl_3): δ 150.3, 140.4, 138.8, 132.5, 129.1, 126.9, 124.1, 115.8, 43.3, 38.8, 35.6, 27.9, 25.2, 22.7, 22.7. Anal Calcd for $\text{C}_{15}\text{H}_{21}\text{NO}_2$: C, 72.84; H, 8.56; N, 5.66. Found: C, 72.61; H, 8.36; N, 5.52. $[\alpha]_D^{20} -10.3^\circ$ ($c = 1.00$, CHCl_3) for a 95% ee sample.

The optical purity is determined by chiral GLC analysis (Chiraldex-GTA, 140 $^\circ\text{C}$, 15 psi); chromatograms are illustrated below:

Authentic racemic

Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	36.051	MM	0.5305	2.44614e5	7685.19434	50.06920
2	38.200	MM	0.5385	2.43938e5	7549.35791	49.93080

from catalytic reaction

Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	35.584	MM	0.5579	1.13713e5	3396.82300	97.36600
2	37.631	MM	0.4397	3076.22778	116.59928	2.63400

(R)-(-)-3-(4-Nitrophenyl)-1-pentene (6.1:1 mixture of $\text{S}_{\text{N}}2'$ to $\text{S}_{\text{N}}2$ products). IR (neat): 3074 (w), 2962 (m), 2924 (m), 2867 (m), 1596 (m), 1527 (s), 1350 (s), 1111 (m), 853 (s) cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 8.16 (2H, d, $J = 8.8$ Hz, ArH), 7.34 (2H, d, $J = 8.8$ Hz, ArH), 5.91 (1H, ddd, $J = 17.2, 10.4, 7.6$ Hz, $\text{CHCH}=\text{CH}_2$), 5.12-5.04 (2H, m, $\text{CHCH}=\text{CH}_2$), 3.27 (1H, ddd, $J = 7.6, 7.6, 7.6$ Hz, $\text{CHCH}=\text{CH}_2$), 1.86-1.68 (2H, m, CHCH_2CH_3), 0.88 (3H, dd, $J = 7.2, 7.2$ Hz, CHCH_2CH_3). ^{13}C NMR (100 MHz, CDCl_3): δ 152.4, 140.6, 128.6, 123.9, 115.7, 51.7, 28.4, 12.1. Anal Calcd for $\text{C}_{11}\text{H}_{13}\text{NO}_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.34; H, 6.85; N, 7.36. $[\alpha]_D^{20} -50.3^\circ$ ($c = 0.873$, CHCl_3) for a 94% ee sample.

The optical purity is determined by chiral GLC analysis (α -dex, 105 $^\circ\text{C}$, 15 psi); chromatograms are illustrated below:

Authentic racemic

from catalytic reaction

Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	176.040	MF	1.2789	9.30907e4	1213.12329	49.21221
2	178.946	FM	1.2973	9.60711e4	1234.23499	50.78779

Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	177.701	MF	1.3986	2.73753e5	3262.13916	97.01988
2	180.527	FM	1.1031	8408.77539	127.05064	2.98012

(R)-(-)-3-(2-Methylphenyl)-1-pentene (1:1 mixture of S_N2' to S_N2 products). IR (neat): 3081 (m), 2962 (s), 2930 (s), 2873 (m), 1495 (m), 1463 (s), 1381 (m), 966 (s), 903 (m), 746 (s) cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.19-7.08 (4H, m, ArH), 5.90 (1H, ddd, *J* = 17.2, 10.4, 7.2 Hz, CHCH=CH₂), 5.04-4.96 (2H, m, CHCH=CH₂), 3.41 (1 H, ddd, *J* = 7.6, 7.6, 7.6 Hz, CHCH=CH₂), 2.34 (3H, s, ArCH₃), 1.83-1.67 (2H, m, CHCH₂CH₃), 0.91 (3H, dd, *J* = 7.2, 7.2 Hz, CHCH₂CH₃). ¹³C NMR (100 MHz, CDCl₃) (1:1 mixture of S_N2':S_N2): δ 142.6, 141.9, 137.2, 136.1, 135.0, 132.5, 130.4, 130.3, 127.9, 126.9, 126.5, 126.3, 126.1, 125.9, 125.6, 114.1, 46.9, 35.6, 28.0, 22.8, 20.0, 19.8, 13.8, 12.4. HRMS Calcd for C₁₂H₁₆: 160.1252. Found: 160.1251. [α]_D²⁰ -15.4° (*c* = 0.933, CHCl₃) for a 96% ee sample.

The optical purity is determined by chiral GLC analysis (Chiraldex-GTA, 50 °C, 15 psi); chromatograms are illustrated below:

Authentic racemic

from catalytic reaction

Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	106.290	MF	1.9815	8.28039e4	696.48260	49.09231
2	111.532	FM	2.2186	8.58659e4	645.03528	50.90769

Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	108.713	MF	2.0856	1.02879e5	822.12677	98.01221
2	115.527	FM	1.0150	2086.49829	34.26048	1.98779

(R)-(-)-3-(2-Naphthyl)-1-pentene (1:1.5 mixture of S_N2' to S_N2 products). IR (neat): 3043 (m), 2962 (s), 2937 (s), 2880 (m), 1646 (w), 1590 (m), 1514 (m), 1451 (m), 1402 (m), 973 (s), 922 (m), 790 (s) cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 8.14 (1H, d, *J* = 7.6 Hz, ArH), 7.87-7.83 (1H, m, ArH),

7.76-7.72 (1H, m, ArH), 7.53-7.38 (4H, m, ArH), 6.08 (1H, ddd, $J = 17.2, 9.6, 7.2$ Hz, CHCH=CH₂), 5.13-5.08 (2H, m, CHCH=CH₂), 4.02 (1 H, ddd, $J = 7.2, 7.2, 7.2$ Hz, CHCH=CH₂), 1.93 (2H, dqd, $J = 7.6, 7.6, 1.6$ Hz, CHCH₂CH₃), 0.97 (3H, dd, $J = 7.6, 7.6$ Hz, CHCH₂CH₃). ¹³C NMR (100 MHz, CDCl₃) (1:1.5 mixture of S_N2':S_N2): δ 141.9, 140.6, 136.0, 134.5, 133.8, 131.3, 129.1, 128.6, 127.3, 127.2, 126.8, 125.9, 125.8, 125.7, 125.6, 125.4, 124.1, 123.7, 123.6, 114.8, 46.2, 35.7, 28.2, 22.7, 13.9, 12.5. HRMS Calcd for C₁₅H₁₆: 196.1252; Found: 196.1252. $[\alpha]_D^{20} +6.7^\circ$ ($c = 0.60$, CHCl₃) for a 93% ee sample.

The optical purity is determined by chiral HPLC analysis (Chiral Technologies Chiralcel OJ, 254 nm, 100% hexanes, 1 mL/min); chromatograms are illustrated below:

Authentic racemic

from catalytic reaction

PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	29.124		0.0000	0.000	2275429.0	49.708	BB	1.142	33220.48	56.190
2	35.627		0.0000	0.000	2302187.0	50.292	BB	1.481	25901.21	43.810

PK#	Ret Time	Name	Amount	Amount%	Area	Area%	Type	Width	Height	Height%
1	29.502		0.0000	0.000	33667.4	3.319	BB	0.910	616.92	4.859
2	35.713		0.0000	0.000	980858.1	96.681	BB	1.353	12079.75	95.141

(R)-(-)-3-Methyl-3-phenyl-1-pentene. IR (neat): 3081 (w), 3056 (w), 3025 (w), 2968 (s), 2924 (m), 2880 (m), 1646 (w), 1596 (w), 1495 (m), 1445 (m), 1382 (m), 998 (m), 910 (s), 765 (s), 708 (s) cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.34-7.17 (5H, m, ArH), 6.03 (1H, dd, $J = 17.6, 10.8$ Hz, CCH=CH₂), 5.11 (1H, dd, $J = 10.8, 1.6$ Hz, CCH=CH₂), 5.05 (1H, dd, $J = 17.6, 1.6$ Hz, CCH=CH₂), 1.89-1.72 (2H, m, CCH₂CH₃), 1.39 (3H, s, CCH₃), 0.77 (3H, dd, $J = 7.6, 7.6$ Hz, CCH₂CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 147.6, 147.1, 128.2, 126.9, 125.8, 111.9, 44.7, 33.6, 24.5, 9.1. HRMS Calcd for C₁₂H₁₆: 160.1252. Found: 160.1256. $[\alpha]_D^{20} -12.5^\circ$ ($c = 0.800$, CHCl₃) for a 92% ee sample. **Proof of Stereochemistry:** literature value ($[\alpha]_D^{26} +4.55^\circ$ ($c = 1.1$, CHCl₃)) is assigned to the (S) enantiomer.⁵

The optical purity is determined by chiral GLC analysis (β -dex, 80 °C, 15 psi); chromatograms are illustrated below:

⁵ A. Yanagisawa, N. Nomura, Y. Yamada, H. Hibino, H. Yamamoto, *Synlett*. **1995**, 841-842.

Authentic racemic

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	57.640	MM	0.4576	171.98801	6.26370	50.54740
2	59.780	MM	0.4878	168.26291	5.74878	49.45260

from catalytic reaction

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	57.438	MM	0.5147	534.87573	17.32023	95.83587
2	59.988	MM	0.4882	23.24072	7.93420e-1	4.16413

(R)-(-)-3-Methyl-3-(4-trifluoromethylphenyl)-1-pentene. IR (neat): 2974 (m), 2936 (m), 2880 (m), 1621 (m), 1337 (s), 1174 (s), 1130 (s), 1073 (s), 1017 (m), 922 (m), 841 (s) cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 7.54 (2H, d, $J = 8.4$ Hz, ArH), 7.42 (2H, dd, $J = 8.4, 0.8$ Hz, ArH), 6.00 (1H, dd, $J = 17.2, 10.8$ Hz, CCH=CH₂), 5.15 (1H, dd, $J = 10.8, 1.2$ Hz, CCH=CH₂), 5.06 (1H, dd, $J = 17.2, 1.2$ Hz, CCH=CH₂), 1.88-1.75 (2H, m, CCH₂CH₃), 1.37 (3H, s, CCH₃), 0.76 (3H, dd, $J = 7.2, 7.2$ Hz, CCH₂CH₃). ^{13}C NMR (100 MHz, CDCl_3): δ 151.8, 146.1, 127.3, 125.1 (q, $J = 3.8$ Hz, CF₃), 123.2, 112.8, 44.9, 33.5, 24.5, 9.0. HRMS Calcd for C₁₃H₁₅F₃: 228.1126. Found: 228.1128. $[\alpha]_D^{20} -14.2^\circ$ ($c = 1.07$, CHCl_3) for a 88% ee sample.

The optical purity is determined by chiral GLC analysis (β -dex, 110 $^\circ\text{C}$, 15 psi); chromatograms are illustrated below:

Authentic racemic

Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	13.870	MF	0.2335	2.67442e5	1.90914e4	49.84804
2	14.505	FM	0.2752	2.69073e5	1.62967e4	50.15196

from catalytic reaction

Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	13.756	MF	0.2840	6.18703e5	3.63065e4	93.87013
2	14.578	FM	0.2628	4.04023e4	2562.48608	6.12987

(R)-(-)-3-Methyl-3-(4-nitrophenyl)-1-pentene. IR (neat): 3081 (w), 2967 (m), 2936 (m), 2880 (m), 1590 (m), 1520 (s), 1350 (s), 1117 (m), 1017 (m), 916 (m), 853 (s) cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 8.15 (2H, d, $J = 8.8$ Hz, ArH), 7.47 (2H, d, $J = 8.8$ Hz, ArH), 6.00 (1H, dd, $J = 17.6, 10.8$ Hz, CCH=CH₂), 5.18 (1H, dd, $J = 10.8, 1.2$ Hz, CCH=CH₂), 5.08 (1H, dd, J

= 17.6, 1.2 Hz, CCH=CH₂), 1.91-1.75 (2H, m, CCH₂CH₃), 1.39 (3H, s, CCH₃), 0.77 (3H, dd, $J = 7.6, 7.6$ Hz, CCH₂CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 155.5, 145.4, 127.8, 123.4, 112.4, 45.3, 33.6, 24.5, 8.9. Anal Calcd for C₁₂H₁₅NO₂: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.21; H, 7.16; N, 6.67. $[\alpha]_D^{20} -25.1^\circ$ ($c = 1.13$, CHCl₃) for a 87% ee sample.

The optical purity is determined by chiral GLC analysis (β-dex, 130 °C, 15 psi); chromatograms are illustrated below:

Authentic racemic

Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	96.597	MF	1.2837	2.40808e5	3126.59204	50.14744
2	100.057	FM	1.5253	2.39392e5	2615.86084	49.85256

from catalytic reaction

Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	93.473	MF	1.9758	6.51370e5	5494.62598	93.57330
2	99.272	FM	1.7668	4.47367e4	422.00772	6.42670

(R)-(-)-3,7-Dimethyl-3-(4-nitrophenyl)-1-octene. IR (neat): 3081 (w), 2949 (br), 2861 (w), 1596 (m), 1527 (s), 1464 (m), 1350 (s), 1111 (m), 1011 (m), 916 (m), 841 (s) cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 8.15 (2H, d, $J = 9.2$ Hz, ArH), 7.47 (2H, d, $J = 9.2$ Hz, ArH), 6.00 (1H, dd, $J = 17.6, 10.8$ Hz, CCH=CH₂), 5.17 (1H, dd, $J = 10.8, 1.2$ Hz, CCH=CH₂), 5.07 (1H, dd, $J = 17.6, 1.2$ Hz, CCH=CH₂), 1.80-1.68 (2H, m, aliphatic CH), 1.50-1.46 (1H, m, aliphatic CH), 1.40 (3H, s, CCH₃), 1.19-1.06 (4H, br m, aliphatic CH), 0.81 (6H, d, $J = 6.4$ Hz, CH(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃): δ 155.8, 145.7, 127.7, 123.4, 113.2, 45.1, 41.4, 39.6, 27.9, 25.1, 22.7, 22.6, 22.3. Anal Calcd for C₁₆H₂₃NO₂: C, 73.53; H, 8.87; N, 5.36. Found: C, 73.76; H, 8.68; N, 5.26. $[\alpha]_D^{20} -13.0^\circ$ ($c = 1.13$, CHCl₃) for a 83% ee sample.

The optical purity is determined by chiral HPLC analysis (Chiral Technologies Chiralpak AS, 254 nm, 100% hexanes, 0.5 mL/min, $t_{\text{major}} = 21$ min, $t_{\text{minor}} = 24$ min).

(R)-(-)-3-Methyl-3-(4-tolylsulfonyloxyphenyl)-1-pentene. IR (neat): 2962 (m), 2924 (m), 2873 (w), 1596 (m), 1501 (s), 1376 (s), 1180 (s), 1155 (s), 1099 (m), 1023 (m), 872 (s) cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.70 (2H, d, $J = 8.4$ Hz, ArH), 7.30 (2H, d, $J = 8.4$ Hz, ArH), 7.21 (2H, d, $J = 8.8$ Hz, ArH), 6.89 (2H, d, $J = 8.8$ Hz, ArH), 5.94 (1H, dd, $J = 17.6, 10.8$ Hz, CCH=CH₂), 5.09 (1H, dd, $J = 10.8, 1.6$ Hz, CCH=CH₂), 4.99 (1H, dd, $J = 17.6, 1.2$ Hz, CCH=CH₂), 2.44 (3H, s, ArCH₃), 1.82-1.65 (2H, m, CCH₂CH₃), 1.30 (3H, s, CCH₃), 0.72 (3H, dd, $J = 7.6, 7.6$ Hz, CCH₂CH₃). ¹³C NMR (100 MHz, CDCl₃): δ

147.7, 146.6, 146.4, 145.3, 132.8, 129.9, 128.6, 128.1, 121.8, 112.3, 44.5, 33.6, 24.5, 21.8, 8.9. HRMS Calcd for $C_{19}H_{22}O_3S$: 330.1290. Found: 330.1294. $[\alpha]_D^{20} -15.4^\circ$ ($c = 1.00$, $CHCl_3$) for a 88% ee sample.

The optical purity is determined by chiral GLC analysis (β -dex, 120 °C, 15 psi) of the derived acetate, obtained by deprotection of the tosyl moiety, and subsequent acylation; chromatograms are illustrated below:

Authentic racemic

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	125.887	MF	0.3585	488.44400	22.70728	50.17333
2	126.970	FM	0.3845	485.06915	21.02487	49.82667

from catalytic reaction

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	125.707	MF	0.4297	1373.35815	53.26807	93.95374
2	127.178	FM	0.3939	88.38058	3.73915	6.04626

9a CCCCCCCCC/C=C/C (**R**)-(+)-3-Methyldecene. IR (neat): 2968 (s), 2923 (s), 2855 (s), 1457 (w), 992 (w), 903 (m), 671 (m), 645 (w) cm^{-1} . 1H NMR (400 MHz, $CDCl_3$): δ 5.70 (1H, ddd, $J = 17.6, 10.4, 7.6$ Hz, $CHCH=CH_2$), 4.97-4.88 (2H, m, $CHCH=CH_2$), 2.12-2.08 (1H, m, $CHCH=CH_2$), 1.30-1.26 (12H, br m, aliphatic CH), 0.98 (3H, d, $J = 6.8$ Hz, $CHCH_3$), 0.88 (3H, dd, $J = 6.8, 6.8$ Hz, $CH_2CH_2CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.2, 112.3, 37.9, 36.9, 32.1, 29.9, 29.5, 27.4, 22.8, 20.3, 14.3. HRMS Calcd for $C_{11}H_{22}$: 154.1722. Found: 154.1715. $[\alpha]_D^{20} +9.4^\circ$ ($c = 0.53$, $CHCl_3$) for a 78% ee sample.

32 CCCCCCCC[C@H](C)C(=O)C The optical purity is determined by chiral GLC analysis (Chiraldex-GTA, 60 °C, 15 psi) of the derived ketone **26**, obtained by Wacker⁶ oxidation: 1H NMR (400 MHz, $CDCl_3$): δ 2.50 (1H, dddddd, $J = 7.6$ Hz, $CHCHCH_3$), 2.13 (3H, s, $COCH_3$), 1.68-1.60 (1H, m, aliphatic CH), 1.38-1.21 (11H, br m, aliphatic CH), 1.07 (3H, d, $J = 7.2$ Hz, $CHCH_3$), 0.88 (3H, dd, $J = 7.2, 7.2$ Hz, $CH_2CH_2CH_3$); chromatograms are illustrated below:

⁶ a) Y. Ito, T. Hirao, T. Saegusa, *J. Org. Chem.* **1978**, 43, 1011-1013. b) S. J. Degrado, Mizutani, H, A. H. Hoveyda, *J. Am. Chem. Soc.* **2001**, 123, 755-756.

Authentic racemic

Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	49.307	MM	1.5118	7.46361e5	8228.23242	49.89061
2	53.560	MM	1.9099	7.49634e5	6541.54053	50.10939

from catalytic reaction

Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	50.907	MM	0.8149	2.16184e4	442.16782	11.08580
2	54.680	MM	1.2620	1.73391e5	2289.87500	88.91420

(R)-(-)-3-Ethyldecene. IR (neat): 3078 (w), 2965 (m), 2934 (s), 2865 (m), 1466 (w), 1002 (w), 921 (m) cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 5.52 (1H, ddd, $J = 16.8, 10.4, 8.4$ Hz, $\text{CHCH}=\text{CH}_2$), 4.98-4.91 (2H, m, $\text{CHCH}=\text{CH}_2$), 1.85-1.83 (1H, m, $\text{CHCH}=\text{CH}_2$), 1.43-1.19 (14H, br m, aliphatic CH), 0.88 (3H, dd, $J = 6.8, 6.8$ Hz, CH_2CH_3), 0.84 (3H, dd, $J = 7.6, 7.6$ Hz, CH_2CH_3). ^{13}C NMR (100 MHz, CDCl_3): δ 143.6, 114.1, 46.0, 34.8, 32.1, 29.9, 29.5, 27.8, 27.4, 22.8, 14.3, 11.8. Anal Calcd for $\text{C}_{12}\text{H}_{24}$: C, 85.63; H, 14.37. Found: C, 85.29; H, 14.61. $[\alpha]_D^{20} -2.0^\circ$ ($c = 0.80$, CHCl_3) for a 92% ee sample.

The optical purity is determined by chiral GLC analysis (β -dex, 100 $^\circ\text{C}$, 15 psi) of the derived alcohol, obtained by ozonolysis followed by NaBH_4 reduction; chromatograms are illustrated below:

Authentic racemic

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	90.107	MF	1.7868	2364.13159	22.05191	49.93404
2	93.893	FM	2.6794	2370.37769	14.74448	50.06596

from catalytic reaction

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	92.250	MF	0.5515	99.53045	3.00781	3.76936
2	93.495	FM	2.2254	2540.98340	19.02983	96.23064

(R)-(-)-3-ethyl-1-phenyl-1,4-pentadiene (5.7:1 mixture of $\text{S}_{\text{N}}2'$ to $\text{S}_{\text{N}}2$ products). IR (neat): 3081 (m), 3069 (m), 3025 (m), 2967 (s), 2924 (m), 2886 (m), 1646 (m), 1596 (s), 1495 (m), 1457 (m), 992 (s), 966 (s), 929 (s), 765 (s), 690 (m) cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 7.34-7.28 (4H, m, ArH), 7.22-7.18 (1H, m, ArH), 6.39 (1H, d, $J = 16.0$ Hz, ArCH), 6.12 (1H, dd, $J = 16.0$,

7.6 Hz, ArCHCH), 5.80 (1H, ddd, $J = 17.6, 10.4, 7.2$ Hz, CHCH=CH₂), 5.10-5.03 (2H, m, CHCH=CH₂), 2.77 (1 H, ddd, $J = 7.2, 7.2, 7.2$ Hz, CHCH=CH₂), 1.57-1.43 (2H, m, CHCH₂CH₃), 0.93 (3H, dd, $J = 7.2, 7.2$ Hz, CHCH₂CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 141.4, 137.9, 133.2, 129.8, 128.6, 127.1, 126.2, 114.5, 49.0, 27.9, 11.9. HRMS Calcd for C₁₂H₂₀: 164.1567. Found: 164.1566. $[\alpha]_D^{20} -50.1^\circ$ ($c = 0.810$, CHCl₃) for a 89% ee sample.

The optical purity is determined by chiral GLC analysis (β -dex, 80 °C, 20 psi); chromatograms are illustrated below:

Authentic racemic

from catalytic reaction

(R)-(+)-3-Cyclohexyl-1-butene. IR (neat): 2924 (s), 2855 (m), 910 (m), 790 (w), 677 (m), 652 (s) cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 5.52 (1H, ddd, $J = 17.6, 9.6, 8.0$ Hz, CHCH=CH₂), 4.95-4.89 (2H, m, CHCH=CH₂), 1.95 (1H, ddq, $J = 6.8, 6.8, 6.8$ Hz, CHCH=CH₂), 1.74-1.60 (5H, br m, aliphatic CH), 1.26-1.01 (4H, br m, aliphatic CH), 0.96 (3H, d, $J = 6.8$ Hz, CHCH₃), 0.99-0.87 (2H, m, aliphatic CH). ¹³C NMR (100 MHz, CDCl₃): δ 143.8, 113.1, 43.7, 43.0, 30.5, 30.4, 26.8, 26.8, 17.2. Anal Calcd for C₁₀H₁₈: C, 86.88; H, 13.12. Found: C, 86.65; H, 13.33. HRMS Calcd for C₁₀H₁₈: 138.1409. Found: 138.1406. $[\alpha]_D^{20} +13.6^\circ$ ($c = 0.500$, CHCl₃) for a 87% ee sample.

The optical purity of the compound is determined by chiral GLC analysis (β -dex, 100 °C, 15 psi); chromatograms are illustrated below:

Authentic racemic

from catalytic reaction

(R)-(-)-3-Cyclohexyl-1-pentene. IR (neat): 2930 (m), 2855 (m), 992 (w), 910 (m), 678 (s), 652 (s) cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 5.52 (1H, ddd, $J = 16.8, 9.6, 9.2$ Hz, $\text{CHCH}=\text{CH}_2$), 4.99-4.86 (2H, m, $\text{CHCH}=\text{CH}_2$), 1.71-1.61 (6H, br m, aliphatic CH), 1.46 (1H, dqd, $J = 13.3, 7.4, 4.1$ Hz, CHCH_2CH_3), 1.26-0.84 (7H, br m, aliphatic CH), 0.81 (3H, dd, $J = 7.6, 7.6$ Hz, CHCH_2CH_3). ^{13}C NMR (100 MHz, CDCl_3): δ 141.6, 115.1, 52.2, 41.7, 31.3, 29.9, 26.9, 26.9, 26.9, 24.5, 12.2. Anal Calcd for $\text{C}_{11}\text{H}_{20}$: C, 86.76; H, 13.24. Found: C, 86.40; H, 13.50. $[\alpha]_{20}^D -9.2^\circ$ ($c = 0.80$, CHCl_3) for a 95% ee sample.

The optical purity of the compound is determined by chiral GLC analysis (α -dex, 60 $^\circ\text{C}$, 15 psi); chromatograms are illustrated below:

Authentic racemic

Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	34.630	MF	0.3505	2.31647e5	1.10137e4	49.93286
2	35.619	FM	0.4115	2.32270e5	9407.04883	50.06714

from catalytic reaction

Peak #	RetTime [min]	Type	Width [min]	Area counts*s	Height [counts]	Area %
1	34.094	MF	0.3599	1.87453e5	8681.74316	97.57971
2	35.223	FM	0.3711	4649.45117	208.79776	2.42029

(R)-(-)-3-ethyl-decen-4-yne (4.6:1 mixture of $\text{S}_{\text{N}}2'$ to $\text{S}_{\text{N}}2$ products). IR (neat): 2974 (s), 2930 (s), 2867 (m), 1640 (w), 1464 (m), 1382 (w), 1344 (w), 992 (m), 954 (w), 922 (m) cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 5.76 (1H, ddd, $J = 16.8, 10.0, 6.0$ Hz, $\text{CHCH}=\text{CH}_2$), 5.28 (1H, ddd, $J = 16.8, 1.8, 1.8$ Hz, $\text{CHCH}=\text{CHH}$), 5.05 (1H, ddd, $J = 16.8, 1.8, 1.8$ Hz, $\text{CHCH}=\text{CHH}$), 3.00-2.94 (1 H, m, $\text{CHCH}=\text{CH}_2$), 2.20 (2H, ddd, $J = 9.2, 6.8, 2.0$, CH_2CC), 1.62-1.26 (8H, m, aliphatic CH), 0.98 (3H, dd, $J = 7.2, 7.2$ Hz, CH_2CH_3), 0.90 (3H, dd, $J = 7.2, 7.2$ Hz, CH_2CH_3). ^{13}C NMR (100 MHz, CDCl_3): δ 139.0, 114.7, 83.8, 80.5, 37.3, 31.2, 29.0, 28.8, 22.4, 18.9, 14.2, 11.6. HRMS Calc for $\text{C}_{13}\text{H}_{16}$: 172.1248. Found: 172.1252. $[\alpha]_{\text{D}}^{20} -26.2^\circ$ ($c = 0.600$, CHCl_3) for a 96% ee sample.

The optical purity is determined by chiral GLC analysis (β -dex, 58 $^\circ\text{C}$, 15 psi); chromatograms are illustrated below:

Authentic racemic

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	125.621	MF	1.0838	471.41437	7.24914	50.13233
2	128.220	FM	1.3341	468.92560	5.85806	49.86767

from catalytic reaction

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	124.558	MF	1.5740	1322.32336	14.00144	98.04185
2	128.880	FM	1.2839	26.41018	3.42828e-1	1.95815

(R)-(-)-3-Ethyl-3,7-dimethyl-1,6-octadiene. IR (neat): 3078 (w), 2965 (s), 2915 (s), 2877 (m), 2642 (w), 1460 (m), 1385 (m), 1002 (m), 914 (s) cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 5.68 (1H, dd, $J = 17.2$, 10.8 Hz, $\text{CCH}=\text{CH}_2$), 5.11-5.07 (1H, m, $(\text{CH}_3)_2\text{C}=\text{CH}$), 4.93 (2H, ddd, $J = 20.4$, 13.6, 1.6 Hz, $\text{CCH}=\text{CH}_2$), 1.90-1.84 (2H, br m, aliphatic CH), 1.68 (3H, s, $(\text{CH}_3)_2\text{C}=\text{CH}$), 1.59 (3H, s, $(\text{CH}_3)_2\text{C}=\text{CH}$), 1.36-1.26 (4H, m, aliphatic CH), 0.94 (3H, s, CCH_3), 0.79 (3H, d, $J = 7.4$, 7.4 Hz, CCH_2CH_3). ^{13}C NMR (100 MHz, CDCl_3): δ 147.3, 131.1, 125.3, 111.7, 40.6, 39.7, 33.2, 25.8, 23.0, 22.1, 17.7, 8.5. Anal Calcd for $\text{C}_{12}\text{H}_{22}$: C, 86.67; H, 13.33. Found: C, 86.28; H, 13.70. $[\alpha]_D^{20} -18.6^\circ$ ($c = 1.07$, CHCl_3) for a 82% ee sample.

The optical purity is determined by chiral GLC analysis (Chiraldex-GTA, 80 $^\circ\text{C}$, 15 psi) of the derived diacetate, obtained by ozonolysis followed by NaBH_4 reduction and subsequent acylation, $t_{\text{major}} = 317$ min, $t_{\text{minor}} = 324$ min).

(R)-(-)-1-phenyl-3-ethyl-3-methyl-pent-4-en-1-yne. IR (neat): 3081 (m), 3050 (w), 2974 (s), 2923 (s), 2880 (m), 1652 (m), 1615 (m), 1495 (s), 1445 (m), 1394 (m), 1344 (m), 922 (s), 771 (s), 690 (s) cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 7.45-7.41 (2H, m, ArH), 7.31-7.27 (3H, m, ArH), 5.92 (1H, dd, $J = 16.8$, 10.4 Hz, $\text{CCH}=\text{CH}_2$), 5.45-5.40 (1H, m, $\text{CHCH}=\text{CH}_2$), 5.11-5.08 (1H, m, $\text{CHCH}=\text{CH}_2$), 1.67-1.53 (2H, m, CCH_2CH_3), 1.36 (3H, s, CCH_3), 1.00 (3H, dd, $J = 7.2$, 7.2 Hz, CCH_2CH_3). ^{13}C NMR (100 MHz, CDCl_3): δ 143.4, 131.8, 128.3, 127.7, 124.1, 113.3, 93.6, 84.0, 40.0, 35.1, 27.8, 9.8. Anal Calcd for $\text{C}_{14}\text{H}_{16}$: C, 91.25; H, 8.75. Found: C, 90.98; H, 9.00. $[\alpha]_D^{20} -31.8^\circ$ ($c = 1.05$, CHCl_3) for a 91% ee sample.

The optical purity is determined by chiral HPLC analysis (Chiral Technologies Chiralcel OD, 254 nm, 98:2 hexanes:isopropanol, 1 mL/min) of the derived alcohol, obtained by hydroboration with 9-BBN; chromatograms are illustrated below:

Authentic racemic

from catalytic reaction

2-Hydroxy-1-naphthaldehyde- L-Asp(Ot-Bu)-NHn-Bu:

IR (solid film): 3307 (br), 3062 (w), 2968 (m), 2936 (m), 2880 (w), 1741 (m), 1665 (m), 1640 (s), 1539 (m), 1376 (m), 1294 (m), 1243 (m), 1155 (s), 841 (m), 753 (m) cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 9.25 (1H, s, HC=N), 8.07 (1H, d, J = 8.0 Hz, ArH), 7.82 (1H, d, J = 9.2 Hz, ArH), 7.74 (1H, d, J = 8.0 Hz, ArH),

7.53 (1H, ddd, J = 8.0, 8.0, 1.2 Hz, ArH), 7.35 (1H, m, ArH), 7.13 (1H, d, J = 9.2 Hz, ArH), 6.20 (1H, br s, NH), 4.43 (1H, dd, J = 9.2, 3.6 Hz, NCHCO), 3.37-3.22 (2H, m, NCH₂), 3.16 (1H, dd, J = 16.4, 3.6 Hz, CHCHHCO), 2.80 (1H, dd, J = 16.4, 9.2 Hz, CHCHHCO), 1.52-1.45 (2H, m, aliphatic CH), 1.36 (9H, s, *t*-Bu), 1.40-1.25 (2H, m, aliphatic CH), 0.90 (3H, t, J = 7.2 Hz, CH₃). ^{13}C NMR (100 MHz, CDCl_3): δ 170.2, 170.0, 165.4, 165.3, 135.9, 132.9, 129.4, 128.3, 127.7, 123.8, 120.5, 119.3, 108.6, 81.6, 68.9, 40.1, 39.6, 31.7, 28.1, 20.1, 13.8. HRMS Calcd for $\text{C}_{23}\text{H}_{30}\text{N}_2\text{O}_4\text{Na}$ ($\text{M}+\text{Na}^+$): 421.2101. Found: 421.2101.

2-Hydroxy-1-naphthaldehyde- L-Asp (Ot-Bu)-D-Leu-

NHn-Bu: IR (solid film): 3283 (br), 3056 (w), 2962 (m), 2936 (m), 1741 (m), 1652 (s), 1552 (m), 1376 (m), 1300 (w), 1256 (w), 1155 (m), 840 (w), 753 (w) cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 9.27 (1H, s, HC=N), 8.06 (1H, d, J = 8.4 Hz, ArH), 7.84 (1H, d, J = 9.2 Hz, ArH), 7.76 (1H,

d, J = 7.2 Hz, ArH), 7.54 (1H, ddd, J = 7.2, 7.2, 1.2 Hz, ArH), 7.37 (1H, ddd, J = 7.2, 7.2, 1.2 Hz, ArH), 7.15 (1H, d, J = 9.2 Hz, ArH), 6.95 (1H, dd, J = 4.8, 4.8 Hz, NH), 6.45 (1H, d, J = 8.4 Hz, NH), 4.53-4.47 (1H, m, NCHCO), 4.35 (1H, dd, J = 4.8, 4.8 Hz, NCHCO), 3.32-3.18 (2H, m, NCH₂), 3.18 (1H, dd, J = 16.4, 5.6 Hz, CHCHHCO), 2.88 (1H, dd, J = 16.4, 4.8 Hz, CHCHHCO), 1.87-1.81 (1H, m, aliphatic CH), 1.58-1.45 (4H, m, aliphatic CH), 1.42 (9H, s, *t*-Bu), 1.33 (2H, dddddd, J = 7.2, 7.2, 7.2, 7.2, 7.2 Hz, aliphatic CH), 0.91 (3H, dd, J = 7.2, 7.2 Hz, CH₃), 0.87 (3H, d, J = 6.4 Hz, CH(CH₃)₂), 0.84 (3H, d, J = 6.4 Hz, CH(CH₃)₂). ^{13}C NMR (100 MHz, CDCl_3): δ 171.3, 170.6, 170.4, 164.8, 164.5, 136.0, 132.8, 129.4, 128.3, 127.8, 123.9, 120.3, 119.2, 108.6, 82.2, 68.7, 52.3, 40.6, 40.0, 39.6, 31.7, 28.1, 25.2, 23.1, 21.9, 20.2, 13.9. HRMS Calcd for $\text{C}_{29}\text{H}_{41}\text{N}_3\text{O}_5\text{Na}$ ($\text{M}+\text{Na}^+$): 534.2944. Found: 534.2949.

2-Hydroxy-1-naphthaldehyde- Gly -L- Leu-NHn-Bu: IR (solid film): 3264 (br), 3069 (w), 2955 (m), 2917 (m), 2873 (w), 1646 (s), 1540 (m), 1375 (m), 1237 (m), 1193 (m), 841 (w), 740 (w), 715 (w) cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 9.10 (1H, s, $\text{HC}=\text{N}$), 8.00 (1H, d, $J = 8.4$ Hz, ArH), 7.79 (1H, d, $J = 9.2$ Hz, ArH), 7.72 (1H, d, $J = 7.2$ Hz, ArH), 7.50 (1H, dd, $J = 7.2, 7.2$ Hz, ArH), 7.33 (1H, dd, $J = 7.2, 7.2$ Hz, ArH), 7.09 (1H, d, $J = 9.6$ Hz, ArH), 6.63 (1H, d, $J = 8.0$ Hz, NH), 6.15 (1H, br s, NH), 4.50-4.35 (3H, m, NCHCO), 3.32-3.16 (2H, m, NCH_2), 1.74-1.44 (5H, br m, aliphatic CH), 1.32 (2H, dddddd, $J = 7.6, 7.6, 7.6, 7.6, 7.6$ Hz, aliphatic CH), 0.93 (6H, d, $J = 6.0$ Hz, $\text{CH}(\text{CH}_3)_2$), 0.90 (3H, dd, $J = 7.6, 7.6$ Hz, CH_3). ^{13}C NMR (100 MHz, CDCl_3): δ 171.4, 168.7, 167.3, 163.7, 136.3, 133.0, 129.4, 128.2, 127.5, 123.7, 121.3, 119.1, 108.5, 60.6, 52.1, 41.2, 39.5, 31.7, 25.0, 22.9, 22.5, 20.2, 13.8. HRMS Calcd for $\text{C}_{23}\text{H}_{31}\text{N}_3\text{O}_3\text{Na}$ ($\text{M}+\text{Na}^+$): 420.2263. Found: 420.2263.

2-Hydroxy-1-naphthaldehyde- L-Asp (Ot-Bu)- Gly-NHn-Bu: IR (solid film): 3295 (br), 3056 (w), 2968 (m), 2943 (m), 2880 (w), 1728 (m), 1671 (s), 1650 (s), 1552 (m), 1369 (m), 1155 (m), 909 (w), 847 (w), 740 (m) cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 9.27 (1H, s, $\text{HC}=\text{N}$), 8.05 (1H, d, $J = 8.4$ Hz, ArH), 7.83 (1H, d, $J = 9.2$ Hz, ArH), 7.75 (1H, d, $J = 8.0$ Hz, ArH), 7.53 (1H, ddd, $J = 6.8, 6.8, 1.2$ Hz, ArH), 7.36 (1H, ddd, $J = 7.2, 7.2, 0.8$ Hz, ArH), 7.13 (1H, d, $J = 7.2$ Hz, ArH), 6.93 (1H, br s, NH), 6.82 (1H, br s, NH), 4.33 (1H, dd, $J = 4.8, 4.8$ Hz, NCHCO), 4.21 (1H, dd, $J = 16.4, 7.2$ Hz, NCHHCO), 3.71 (1H, dd, $J = 16.4, 4.8$ Hz, NCHHCO), 3.33-3.16 (3H, m, NCH_2 and CHCHHCO), 2.89 (1H, dd, $J = 16.4, 4.8$ Hz, CHCHHCO), 1.55-1.46 (2H, br m, aliphatic CH), 1.49 (9H, s, $t\text{-Bu}$), 1.39-1.25 (2H, m, aliphatic CH), 0.90 (3H, dd, $J = 7.2, 7.2$ Hz, CH_3). ^{13}C NMR (100 MHz, CDCl_3): δ 171.0, 170.4, 168.5, 164.8, 164.8, 136.0, 132.8, 129.4, 128.3, 127.8, 123.9, 120.3, 119.2, 108.7, 82.3, 68.8, 43.5, 40.0, 39.6, 31.6, 28.2, 20.2, 13.9. HRMS Calcd for $\text{C}_{25}\text{H}_{33}\text{N}_3\text{O}_5\text{H}$ ($\text{M}+\text{H}^+$): 456.2498. Found: 456.2496.

2-Hydroxy-1-naphthaldehyde- L-Asp (Ot-Bu)-L-Leu(NMe)-NHn-Bu: IR (solid film): 3396 (br), 3320 (m), 3056 (w), 2968 (s), 2930 (s), 2886 (m), 1728 (m), 1665 (s), 1646 (s), 1545 (m), 1483 (m), 1369 (s), 1162 (s), 841 (m), 759 (m), 734 (m) cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 9.20 (1H, s, $\text{HC}=\text{N}$), 7.96 (1H, d, $J = 8.4$ Hz, ArH), 7.79 (1H, d, $J = 8.8$ Hz, ArH), 7.71 (1H, d, $J = 8.0$ Hz, ArH), 7.48 (1H, ddd, $J = 6.8, 6.8, 1.2$ Hz, ArH), 7.32 (1H, ddd, $J = 8.0, 8.0, 0.8$ Hz, ArH), 7.08 (1H, d, $J = 8.8$ Hz, ArH), 6.50 (1H, dd, $J = 5.6, 5.6$ Hz, NH), 5.32 (1H, dd, $J = 10.4, 4.8$ Hz, NCHCO), 5.07 (1H, dd, $J = 9.6, 4.0$ Hz, NCHCO), 3.35-3.15 (2H, m, NCH_2), 3.29 (1H, dd, $J = 16.8, 9.6$ Hz, CHCHHCO), 3.01 (3H, s, NCH_3), 2.80 (1H, dd, $J = 16.8, 4.8$ Hz, CHCHHCO), 1.90-1.83 (1H, m, aliphatic CH), 1.68-1.60 (1H, m, aliphatic CH), 1.56-1.47 (2H, m, aliphatic CH), 1.45 (9H, s, $t\text{-Bu}$), 1.34-1.25 (3H, m, aliphatic CH), 0.92 (3H, dd, $J = 7.2, 7.2$ Hz, CH_3), 0.91 (6H, d, $J = 6.8$ Hz, $\text{CH}(\text{CH}_3)_2$), 0.85 (3H, d, $J = 6.8$ Hz, $\text{CH}(\text{CH}_3)_2$). ^{13}C NMR (100 MHz, CDCl_3): δ 171.4, 170.8, 170.2, 167.0, 161.0, 135.9, 133.0, 129.4,

128.0, 127.5, 123.6, 121.3, 119.0, 108.5, 82.1, 60.1, 55.3, 39.6, 36.0, 31.8, 30.7, 28.2, 25.1, 23.5, 21.7, 20.3, 13.9. HRMS Calcd for $C_{30}H_{43}N_3O_5H$ ($M+H^+$): 526.3281. Found: 526.3282.

2-Hydroxy-1-naphthaldehyde- L-Asp (Ot-Bu)-NH(4-(S)-2-methyl-5-decene): IR (solid film): 3283 (br), 3069 (w), 2962 (m), 2924 (m), 2880 (w), 1741 (m), 1653 (m), 1640 (s), 1552 (m), 1376 (m), 1161 (m), 972 (w), 853 (m), 752 (m) cm^{-1} . 1H NMR (400 MHz, $CDCl_3$): δ 9.26 (1H, s, HC=N), 8.08 (1H, d, $J = 7.6$ Hz, ArH), 7.84 (1H, d, $J =$

9.2 Hz, ArH), 7.75 (1H, d, $J = 8.0$ Hz, ArH), 7.54 (1H, ddd, $J = 7.2, 7.2, 1.2$ Hz, ArH), 7.36 (1H, ddd, $J = 7.2, 7.2, 1.2$ Hz, ArH), 7.14 (1H, d, $J = 9.2$ Hz, ArH), 5.94 (1H, d, $J = 7.6$ Hz, NH), 5.55 (1H, ddd, $J = 15.2, 6.8, 6.8$ Hz, CH=CHCH₂), 5.24 (1H, dd, $J = 15.2, 6.8$ Hz, CH=CHCH₂), 4.52-4.39 (2H, m, NCHCO and NCHCH=CH), 3.17 (1H, dd, $J = 16.4, 3.6$ Hz, CHCHHCO), 2.79 (1H, dd, $J = 16.4, 9.6$ Hz, CHCHHCO), 1.93 (2H, ddd, $J = 6.8, 6.8, 6.8$ Hz, CHCH₂), 1.65-1.57 (1H, m, aliphatic CH), 1.45-1.16 (6H, m, aliphatic CH), 1.35 (9H, s, *t*-Bu), 0.92 (6H, d, $J = 6.8$ Hz, CH(CH₃)₂), 0.80 (3H, dd, $J = 7.2, 7.2$ Hz, CH₃). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 169.2, 165.4, 164.3, 135.9, 132.9, 132.3, 129.8, 129.4, 128.3, 127.8, 123.8, 120.5, 119.4, 108.7, 81.6, 69.0, 49.8, 44.6, 40.1, 32.0, 31.3, 28.2, 25.0, 22.8, 22.7, 22.3, 14.0. HRMS Calcd for $C_{30}H_{42}N_2O_4H$ ($M+H^+$): 495.3223. Found: 495.3221.

2-Hydroxy-1-naphthaldehyde- L-Asp (Ot-Bu)-L-Leu-OMe:

IR (solid film): 3301 (br), 3056 (w), 2967 (m), 2924 (m), 2880 (w), 1741 (m), 1678 (m), 1640 (s), 1552 (m), 1376 (m), 1161 (m), 916 (w), 841 (m), 746 (m) cm^{-1} . 1H NMR (400 MHz, $CDCl_3$): δ 9.29 (1H, s, HC=N), 8.07 (1H, d, $J = 8.4$ Hz, ArH), 7.82 (1H, d, $J = 8.4$ Hz, ArH), 7.74 (1H, d, $J = 8.0$ Hz, ArH), 7.53 (1H, ddd, $J = 7.2, 7.2, 1.2$ Hz, ArH), 7.35 (1H, dd, $J = 7.2, 7.2$ Hz, ArH), 7.14 (1H, d, $J = 8.4$ Hz, ArH), 6.54 (1H, d, $J = 8.8$ Hz, NH), 4.64 (1H, m, NCHCO), 4.48 (1H, dd, $J = 8.8, 3.6$ Hz, NCHCO), 3.68 (3H, s, OCH₃), 3.15 (1H, dd, $J = 16.4, 4.0$ Hz, CHCHHCO), 2.82 (1H, dd, $J = 16.4, 9.2$ Hz, CHCHHCO), 1.72-1.56 (3H, br m, aliphatic CH), 1.36 (9H, s, *t*-Bu), 0.95 (6H, d, $J = 6.0$ Hz, CH(CH₃)₂). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.1, 170.2, 169.8, 165.3, 164.8, 135.9, 132.9, 129.3, 128.2, 127.7, 123.8, 120.4, 119.4, 108.7, 81.7, 68.5, 52.5, 51.1, 41.3, 40.0, 28.1, 25.1, 22.9, 22.1. HRMS Calcd for $C_{26}H_{34}N_2O_6Na$ ($M+Na^+$): 493.2311. Found: 493.2315.

2-Hydroxy-1-naphthaldehyde- L-Asp (Ot-Bu)-L-Leu-NMe₂:

IR (solid film): 3283 (br), 3062 (w), 2968 (m), 2943 (m), 2880 (w), 1734 (m), 1653 (m), 1646 (s), 1552 (m), 1420 (m), 1370 (m), 1161 (m), 841 (w), 752 (m) cm^{-1} . 1H NMR (400 MHz, $CDCl_3$): δ 9.26 (1H, s, HC=N), 8.06 (1H, d, $J = 8.8$ Hz, ArH), 7.81 (1H, d, $J = 6.8$ Hz, ArH), 7.73 (1H, dd, $J = 8.0, 1.2$ Hz, ArH), 7.51 (1H, ddd, $J = 6.8, 6.8, 1.2$ Hz, ArH), 7.34 (1H, ddd, $J = 7.2, 7.2, 1.2$ Hz, ArH), 7.14 (1H, d, $J = 8.8$ Hz, ArH), 6.86 (1H, d, $J = 8.0$ Hz, NH),

5.02 (1H, ddd, $J = 10.0, 10.0, 4.0$ Hz, NCHCO), 4.45 (1H, dd, $J = 9.6, 4.0$ Hz, NCHCO), 3.15 (1H, dd, $J = 16.4, 3.6$ Hz, CHCHHCO), 3.08 (3H, s, NCH₃), 2.89 (3H, s, NCH₃), 2.81 (1H, dd, $J = 16.4, 9.6$ Hz, CHCHHCO), 1.71-1.41 (3H, br m, aliphatic CH), 1.35 (9H, s, *t*-Bu), 1.01 (3H, d, $J = 6.8$ Hz, CH(CH₃)₂), 0.93 (3H, d, $J = 6.8$ Hz, CH(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃): δ 172.0, 169.9, 165.5, 164.6, 164.5, 135.7, 133.0, 129.3, 128.1, 127.7, 123.6, 120.7, 119.5, 109.7, 81.6, 68.6, 47.8, 42.3, 20.1, 37.1, 35.9, 28.1, 24.9, 23.6, 22.1. HRMS Calcd for C₂₇H₃N₃O₅H (M+H⁺): 484.2806. Found: 484.2811.

2-Methoxy-1-naphthaldehyde- L-Asp (OtBu)-L-Leu-NHnBu: IR (solid film): 3314 (br), 3068 (m), 2968 (m), 2930 (m), 2867 (m), 1722 (s), 1646 (s), 1539 (s), 1457 (s), 1357 (s), 1237 (s), 1155 (s), 1080 (s), 916 (m), 822 (m), 727 (m) cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 9.07 (1H, s, HC=N), 8.91 (1H, d, $J = 8.8$ Hz, ArH), 7.90 (1H, d, $J =$

9.2 Hz, ArH), 7.76 (1H, d, $J = 8.4$ Hz, ArH), 7.53-7.48 (1H, m, ArH), 7.38-7.34 (1H, m, ArH), 7.26 (1H, d, $J = 8.8$ Hz, ArH), 7.16 (1H, d, $J = 8.0$ Hz, NH), 6.51 (1H, br s, NH), 4.48-4.43 (1H, m, NCHCO), 4.36 (1H, dd, $J = 10.0, 3.2$ Hz, NCHCO), 3.98 (3H, s, OCH₃), 3.23-3.12 (2H, m, NCH₂), 3.08 (1H, dd, $J = 16.0, 3.2$ Hz, CHCHHCO), 2.78 (1H, dd, $J = 16.0, 10.0$ Hz, CHCHHCO), 1.77-1.39 (7H, m, aliphatic CH), 1.36 (9H, s, *t*-Bu), 1.33-1.20 (2H, m, aliphatic CH), 0.93 (3H, d, $J = 7.2$ Hz, CH(CH₃)₂), 0.92 (3H, d, $J = 7.2$ Hz, CH(CH₃)₂), 0.84 (3H, d, $J = 7.2$ Hz, CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 172.5, 171.5, 170.1, 163.2, 158.3, 133.5, 132.2, 129.0, 128.4, 128.2, 125.0, 124.3, 116.5, 112.7, 81.2, 71.0, 56.5, 51.8, 40.3, 39.2, 31.5, 28.1, 25.0, 23.1, 22.2, 20.1, 13.8. HRMS Calcd for C₃₀H₄₃N₃O₅Na (M+Na⁺): 548.3108. Found: 548.3100.

Synthesis of (*R*)-(+)-4-(2-nitrophenyl)-1-(diethylphosphoryloxy)-2-hexene: (*R*)-(+)-3-(2-Nitro-phenyl)-1-pentene (**5e**) (0.11 g, 0.55 mmol includes S_N2 product) and *cis*-2-butene-1,4-diacetate (9.5 x 10⁻² g, 0.55 mmol) are dissolved in 3.5 mL CH₂Cl₂ and Ru-catalyst (3.5 mg, 5.5 x 10⁻² mmol) is added in one portion under a nitrogen atmosphere. After 24 h, the reaction is concentrated *in vacuo*. The resulting brown solution is purified by silica gel column chromatography (5:1 hexanes/EtOAc, R_f product = 0.17) to yield a colorless oil (5.1 x 10⁻² g, 0.19 mmol, 73% based on 58% conversion). (*R*)-(+)-1-Acetoxy-4-(2-nitrophenyl)-2-hexene (8.0 x 10⁻² g, 0.30 mmol) is dissolved in 1.5 mL CH₂Cl₂ followed by the addition of MeOH (0.75 mL) and K₂CO₃ (0.17 g, 1.2 mmol). After 2 h, TLC analysis shows complete conversion to product (1:1 hexanes/EtOAc; R_f starting material = 0.69, R_f product = 0.31). The reaction is quenched by the addition of 5 mL 10% aqueous HCl, and extracted with EtOAc (3 x 3.0 mL). The combined organic layers are dried over anhydrous MgSO₄, filtered, and concentrated to yield a yellow oil which is purified by silica gel column chromatography (5.8 x 10⁻² g, 0.26 mmol, 86%). (*R*)-(+)-4-(2-Nitrophenyl)hex-2-en-1-ol is converted to the derived phosphate by a previously reported procedure.³

(*R*)-(+)-4-(2-Nitrophenyl)-1-(diethylphosphoryloxy)-2-hexene. IR (neat): 3465 (w), 3069 (m), 2962 (s), 2930 (s), 2873 (s), 1665 (w), 1615 (m), 1539 (s), 1464 (m), 1357 (s),

1281 (s), 1162 (s), 1017 (s), 859 (s), 753 (s) cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 7.72 (1H, dd, $J = 8.0, 1.2$ Hz, ArH), 7.54 (1H, dd, $J = 8.0, 8.0, 1.6$ Hz, ArH), 7.39 (1H, dd, $J = 8.0, 1.2$ Hz, ArH), 7.33 (1H, ddd, $J = 8.0, 8.0, 1.2$ Hz, ArH), 5.91 (1H, dd, $J = 15.6, 8.8$ Hz, $\text{CH}=\text{CHCH}_2\text{O}$), 5.64 (1H, dddd, $J = 15.6, 6.0, 6.0, 1.2$ Hz, $\text{CH}=\text{CHCH}_2\text{O}$), 4.52-4.48 (2H, m, $\text{CH}=\text{CHCH}_2\text{O}$), 4.13-4.03 (4 H, m, $\text{PO}_2(\text{OCH}_2\text{CH}_3)$), 3.80 (1H, dd, $J = 7.2, 7.2$ Hz, CHCH_2CH_3), 1.83-1.74 (2H, m, CHCH_2CH_3), 1.30 (6H, dddd, $J = 10.4, 7.2, 7.2, 0.8$ Hz, $\text{PO}_2(\text{OCH}_2\text{CH}_3)$), 0.87 (3H, dd, $J = 7.2, 7.2$ Hz, CHCH_2CH_3). ^{13}C NMR (100 MHz, CDCl_3): δ 150.4, 138.1, 136.7, 132.7, 129.1, 127.2, 126.1 (d, $J = 6.4$ Hz), 124.2, 67.6 (d, $J = 5.3$ Hz), 63.9 (d, $J = 5.0$ Hz), 63.8 (d, $J = 5.5$ Hz), 43.7, 28.6, 16.3 (d, $J = 6.8$ Hz), 12.1. HRMS Calcd for $\text{C}_{16}\text{H}_{24}\text{NO}_6\text{P}$: 357.1341. Found: 357.1344. $[\alpha]_{\text{D}}^{20} +11.1^\circ$ ($c = 2.53$, CHCl_3).

(3R,4R)-(+)-4-(2-Nitrophenyl)-3-methylhexene. IR (neat): 3081 (m), 2962 (s), 2937 (m), 2880 (m), 1532 (s), 1451 (m), 1369 (s), 999 (m), 922 (m), 859 (m), 803 (m), 746 (m) cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 7.63 (1H, dd, $J = 7.6, 1.6$ Hz, ArH), 7.55-7.51 (1H, m, ArH), 7.38 (1H, dd, $J = 7.6, 1.6$ Hz, ArH), 7.31 (1H, ddd, $J = 7.6, 7.6, 1.2$ Hz, ArH), 5.71 (1H, ddd, $J = 17.6, 9.6, 8.8$ Hz, $\text{CHCH}=\text{CH}_2$), 5.05-5.00 (2H, m, $\text{CHCH}=\text{CH}_2$), 2.86 (1 H, ddd, $J = 10.8, 9.2, 3.6$ Hz, CHCH_2CH_3), 2.40-2.30 (1 H, m, $\text{CHCH}=\text{CH}_2$), 1.92 (1H, ddd, $J = 14.0, 7.6, 3.6$ Hz, CHCHHCH_3), 1.47 (1H, ddd, $J = 14.0, 10.8, 7.2$ Hz, CHCHHCH_3), 0.81 (3H, d, $J = 6.8$ Hz, CHCH_3), 0.68 (3H, dd, $J = 7.2, 7.2$ Hz, CCH_2CH_3). ^{13}C NMR (100 MHz, CDCl_3): δ 152.5, 142.6, 138.3, 132.0, 128.4, 126.7, 123.4, 115.0, 46.1, 44.8, 26.9, 19.4, 11.9. HRMS Calcd for $\text{C}_{13}\text{H}_{17}\text{NO}_2$: 219.1259. Found: 219.1258. $[\alpha]_{\text{D}}^{20} +44.3^\circ$ ($c = 0.533$, CHCl_3).

Ligand Optimization Studies:

Representative procedure for synthesis of dipeptide ligand on solid support. Gly-Wang resin (0.10 g , $6.0 \times 10^{-2} \text{ mmol}$) is weighed into a tube and allowed to swell in 2 mL DMF for 8 h. After this time, DMF is removed by filtration, and Fmoc-L-Nle-OH ($8.5 \times 10^{-2} \text{ g}$, 0.24 mmol) is weighed into the tube with the resin. The amino acid is dissolved in 2 mL DMF, followed by addition of DIC ($4.1 \times 10^{-2} \text{ mL}$, $2.7 \times 10^{-2} \text{ mmol}$). The tube is then capped and agitated for 3 h. After this time, the excess reagents are filtered off and the resin is washed eight times with 2 mL of DMF. To deprotect, 2 mL of a 20% solution of piperidine in DMF is added to the tubes. The tubes are then recapped and agitated for 30 min. The solution is filtered off and the resin is washed eight times with 2 mL of DMF. For the second coupling, Fmoc-L-Cha-OH ($9.5 \times 10^{-2} \text{ g}$, 0.24 mmol), 2 mL of DMF, and DIC ($4.1 \times 10^{-2} \text{ mL}$, $2.7 \times 10^{-2} \text{ mmol}$) are added to the tube with the washed resin and the solution is agitated for 3 h. The solution is then filtered, and the resin is washed eight times with 2 mL of DMF. To deprotect, 2 mL of a 20% solution of piperidine in DMF is added to each tube, the tubes recapped and agitated for 30 min. The solution is again filtered and the resin is washed eight times with 2 mL of DMF. Salicyl aldehyde ($4.1 \times 10^{-2} \text{ g}$, 0.24 mmol) and 2 mL of DMF are added to the tube and it is agitated for 48 h. At this time, the solution is filtered and the resin is washed eight times with 2 mL of DMF, eight times with 2 mL of

toluene, and eight times with 2 mL of diethyl ether. Lastly, the resin is treated with 2 mL of a 9:1:0.5 MeOH:DMF:Et₃N solution and agitated for 12 h. At this time the resin is washed with EtOAc (8 x 2 mL). EtOAc is then removed *in vacuo* and 2 mL of toluene are added to the yellow solid and then toluene is also removed. The ligand is dried over P₂O₅ under vacuum for 24 h before use.

Ligand Screening Results.⁷ The screening was carried out using the conversion of **6a** (23 mg, 8.0 x 10⁻² mmol) to **7a** as the test reaction. The reactions were carried out using (CuOTf)₂ · C₆H₆ (2.0 mg, 4.0 x 10⁻³ mmol) and 10 mol % ligand (4.1 mg, 8.0 x 10⁻³ mmol), 3.0 equiv Et₂Zn (25 µL, 2.4 x 10⁻¹ mmol) in 1.0 mL THF at -30 °C for 12 h. The results are depicted for each library screen.

Chart 1. *Ligand Screen for AA₁ Optimization (AA₂ = Nle).* The library indicated Asp(OtBu) is one optimal AA₁ (68% ee).

Chart 2. *Ligand Screen for AA₂ Optimization (AA₁ = Asp(OtBu)).* The library indicated a few amino acids to be optimal AA₂ (83-90% ee). However, once the ligands were made with the solution phase method, Leu as AA₂ was optimal (92% ee).

⁷ B. M. Cole, K. D. Shimizu, C. A. Krueger, J. P. A. Harrity, M. L. Snapper, A. H. Hoveyda, *Angew. Chem., Int. Ed.* **1996**, 35, 1668-1671.

Chart 3. *Ligand Screen for Schiff Base Optimization.* 19 salicyl aldehydes (Scheme 3) were screened. Aldehydes **2** and **10** proved to be optimal (92% ee).

Scheme 4. Aldehydes for Schiff Base Screen